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The hippocampo-cortical loop: Spatio-temporal learning and goal-oriented planning in navigation

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ABSTRACT

We present a neural network model where the spatial and temporal components of a task are merged and learned in the hippocampus as chains of associations between sensory events. The prefrontal cortex integrates this information to build a cognitive map representing the environment. The cognitive map can be used after latent learning to select optimal actions to fulfill the goals of the animal. A simulation of the architecture is made and applied to learning and solving tasks that involve both *spatial and temporal* knowledge. We show how this model can be used to solve the *continuous place navigation task*, where a rat has to navigate to an unmarked goal and wait for 2 seconds without moving to receive a reward. The results emphasize the role of the hippocampus for both spatial and timing prediction, and the prefrontal cortex in the learning of goals related to the task.

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1. Introduction

Spatial navigation relies on a network of strongly interconnected structures that includes the hippocampus, the prefrontal cortex and the basal ganglia. Finding out how information about space, paths, rewards and behavioral control flows between these cerebral structures could shed light on the processes involved in learning complex navigational tasks in the mammalian brain. In this paper, we present a model that attempts to describe how the neural network performs such computations.

From an anatomical point of view, strong excitatory connections exist between the hippocampus and the medial prefrontal cortex (mPFC) in the rat (see Fig. 1). Area CA1 of the ventral hippocampus projects directly to the prelimbic and infralimbic areas of the mPFC (Jay & Witter, 1991). These connections involve both pyramidal neurons and interneurons in the prefrontal cortex. The mPFC projects back to the hippocampus through indirect pathways (Amaral & Witter, 1995). It is connected to the deep layers of the entorhinal cortex which in turn projects to areas CA3 and CA1 through its intermediate and superficial layers (Amaral, Bliss, & O'Keefe, 2006). The nucleus reuniens of the thalamus is also an important relay between the mPFC and the hippocampus (Vertes, Hoover, Szigeti-Buck, & Leranth, 2007). It receives excitatory signals from different structures and mPFC in particular, and

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projects to area CA1. Finally, in the basal ganglia (BG), the striatum receives connections from both the hippocampus and the mPFC. Bilateral connections exist between the BG and mPFC (Groenewegen, Wright, & Uylings, 1997).

In the CA1 and CA3 subregions of the hippocampus, pyramidal neurons called place cells show location-specific firing (O'Keefe & Dostrovsky, 1971). The activity of a place cell is maximal when the animal is at a particular location (the place field) in the environment and decreases as it gets away from it. Thus, the place cell system is believed to allow the animal to locate itself in its environment and is important for the memorization of different environments. Both allothetic (external: visual, olfactory, etc.) and idiothetic (internal: vestibular, somatosensory, etc.) information is used to maintain stable place cell activity. For example, rotation of remote visual cues in a given environment induces equivalent rotation of the place fields (Muller & Kubie, 1987; O'Keefe & Nadel, 1978). Place cells can also be active and show stable place fields when the rat is forced to rely on idiothetic cues in the absence of allothetic cues (e.g., in the dark) (Quirk, Muller, & Kubie, 1990). However, integration of idiothetic information (path integration) allows only limited navigation performance due to error accumulation (Etienne & Jeffery, 2004). Place cell activity has also been shown to be modulated by non spatial information such as olfactory cues (Eichenbaum, Kuperstein, Fagan, & Nagode, 1987), speed, direction, turning angle, trajectory encoding (Wood, Dudchenko, Robitsek, & Eichenbaum, 2000) and other task relevant approach movements (Wiener, Paul, & Eichenbaum, 1989), suggesting a crucial role of the hippocampus in episodic memory (reviews in Eichenbaum, Sauvage, Fortin, Komorowski, & Lipton, 2012; Wiener, 1996).



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Fig. 1. Excitatory connections in the hippocampo-cortical loop. Red connections are those taken into account in the new global model (see Section 3.3). mPFC: medial prefrontal cortex. CA1 and CA3: Cornus amonis. EC: Entorhinal cortex. gc and mc: granule and mossy cells (in dentate gyrus (DG)). RE: Nucleus reuniens. S: Subiculum. A: Amygdala. PER: Perirhinal cortex. POR: Postrhinal cortex. The different layers of EC are indicated by numbers (2 and 3: superficial layers; 5: deep layer). Sensory information mainly comes from PER and POR. Hippocampal output is transferred after S to the basal ganglia.

Source: Adapted from Buzsàki (2007).

Other types of cells with location-specific firing have been found in various regions of the rodent hippocampal system such as the dentate gyrus (DG) and the superficial layers of the entorhinal cortex (EC) (Jung & McNaughton, 1993; Quirk, Muller, Kubie, & Ranck, 1992). More recently, cells with multiple firing fields have been found in the dorsomedial part of the entorhinal cortex (Hafting, Fyhn, Molden, Moser, & Moser, 2005). These "grid cells" show a grid-like firing pattern and have been suggested to implement a path integration-based spatial representation (McNaughton, Battaglia, Jensen, Moser, & Moser, 2006). Grid cells probably have strong functional interactions with hippocampal place cells but these interactions are still poorly understood (Gaussier et al., 2007).

Recently, cells with spatial correlates have been found in the mPFC of the rat performing a goal-oriented task (Hok, Save, Lenck-Santini, & Poucet, 2005). In this experiment, many mPFC cells had a place field at the goal location, i.e. a place with a high motivational salience. Although the mPFC is not required for solving simple navigation tasks, it has been shown to contribute to the acquisition of the optimal behavior to reach a platform in a water maze (de Bruin, Sànchez-Santed, Heinsbroek, Donker, & Postmes, 1994). Lesions of the mPFC also greatly reduce performance in navigation tasks when a certain level of planning and behavioral flexibility is needed (Granon & Poucet, 1995, 2000). The mPFC is also involved in strategy selection as lesions reduce the ability to switch between strategies and lead to increased persistence errors (Ragozzino, Detrick, & Kesner, 1999).

Traditionally, most models of spatial learning in the hippocampus can be divided into two categories. The first category relies on recurrent connections in CA3, which acts as an auto-associative map where attractors are learned to form representations of EC input. Recurrent connections allow to connect consecutively experienced spatial patterns where each pattern corresponds to one location. As a result a spatial graph of the environment is created (Muller, Stead, & Pach, 1996; O'Keefe & Nadel, 1978) in which a given spatial pattern is able to activate another spatial pattern. Such models have been used to simulate place cell activity (Káli & Dayan, 2000) and to solve goal-oriented navigation tasks (Koene, Gorchetchnikov, Cannon, & Hasselmo, 2003; Redish & Touretzky, 1998). The second type of model relies on DG to perform pattern separation. The role of DG in pattern separation is supported by in-vitro and in-vivo studies (review in Acsady & Kali, 2007). DG is suggested to be a highly competitive network that allows a sparse coding of EC information using population coding. Its role in spatial pattern separation has led researchers to hypothesize its involvement in the formation of spatial patterns in the hippocampus from grid cell information (Fyhn, Hafting, Treves, Moser, & Moser, 2007; Rolls, Stringer, & Elliot, 2006) and to suggest that it is part of a system capable of encoding time and space on numerous different scales (Gorchetchnikov & Grossberg, 2007). The model presented in this paper can be included in the latter category since the spatial code built in the hippocampus relies on spatial input from both EC and DG.

In addition to their spatial correlates, both hippocampal place cells and mPFC goal cells have recently been shown to display timerelated activity (Harvey, Coen, & Tank, 2012; Hok et al., 2007). For instance, mPFC neurons and hippocampal neurons were found to increase their firing just before the end of a two seconds waiting period at a goal location (Burton, Hok, Save, & Poucet, 2009) (see Section 2). Internally generated continually changing cell assemblies were found during the delay period of a memory task (Pastalkova, Itskov, Amarasingham, & Buzsáki, 2008). We have also different cells for different spatial inputs and sequences. However, the model presented in this paper stays "focused" on the task. The activity during a delay period reflects both the prediction of the ending time of the waiting period and the spatial location of the animal. Recent results by McDonald, Lepage, Eden, and Eichenbaum (2011) show that similarly to place cells, time cells fire during temporal gaps between events. Moreover, they show that neurons in the hippocampus respond to spatial and/or temporal events.

Here, we present a model in which such timed associations between sensory events as well as spatial correlates are learned in the hippocampus. Multi-modal information is integrated in the entorhinal cortex to characterize these perceptive events. The model can then predict reachable states in terms of space and time. We suggest that the temporal activity recorded in hippocampal place cells and prefrontal neurons reflects these predictions. We show how the mPFC can use this information to control the strategies involved in action selection.

We first present experimental evidence on the continuous place navigation task (see Section 2). The detailed architecture and equations of the neural network are then presented (see Section 3) before giving experimental results of an implementation on a simulated robot navigating in an open environment (see Section 4). Finally we discuss the results (see Section 5).

2. Experimental evidence on the continuous place navigation task

Previously, we have demonstrated that mPFC neurons recorded as the rat performed the *continuous place navigation task* display goal firing (Hok et al., 2005; Lenck-Santini, Muller, Save, & Poucet, 2002). This task consists of 3 phases that are repeated as long as the experiment lasts:

- 1. The rat must reach an unmarked goal location in an open arena with a single polarizing cue card (navigation).
- 2. At the goal location, the rat must stay immobile for 2 s (delay). A food pellet is then delivered by a dispenser above the arena. As it bounces when hitting the ground, the food pellet can end anywhere in the arena.
- 3. The rat must explore the arena to find the food pellet (foraging).

Interestingly, the continuous place navigation task combines both spatial and temporal components. It also allows dissociation of the spatial and temporal correlates of cell firing. The fact that the animal is immobile during the waiting period can disambiguate the behavioral origin of the changes observed in neural activity. Furthermore, this task is also relevant from an action selection perspective. Since the animal must be able (i) to navigate towards an unmarked spatial goal location, (ii) to control its movement for the duration of the delay while at the goal location, and (iii) to explore its environment, the task taxes a variety of behavioral strategies. More importantly, a simple sensorimotor strategy is insufficient to solve the continuous place navigation task. Planning is necessary.

In this task, many mPFC neurons fire when the rat is located at specific, salient spatial locations such as the goal location. Since mPFC neurons recorded from rats simply exploring the arena do not display any spatial activity (Poucet, 1997), a plausible explanation of the firing patterns observed in the continuous navigation task is that mPFC neurons code places with a high motivational salience.

The continuous place navigation task was also used to record hippocampal place cell activity (Hok et al., 2007, 2007). Hippocampal place fields were distributed over the entire arena and did not over-represent the goal location. Interestingly, most place cells displayed excess firing activity at the goal location which, from a purely spatial perspective, looked like a secondary place field (see Fig. 2). Closer scrutiny of the characteristics of excess firing at the goal, however, revealed that it peaked just before the end of the 2 s delay. Since the rat is immobile at that time, no motor commands or changes in its location can account for such a transitory firing peak. This firing pattern suggests instead that excess firing at the goal is linked with reward expectation, and thus is time-related rather than location-related. That rats estimate the duration of the 2 s delay is supported by the observation that when no food was given after a correct response (extinction trials), they resumed their movement precisely at the end of 2 s period of immobility even in the absence of the sound produced by the food dispenser (Hok et al., 2007). This demonstrates their ability to estimate the elapsed waiting time and thus to learn the timing required for obtaining the reward. The temporal component of hippocampal goal-related activity may therefore reflect the manifestation of a prediction mechanism.

To determine if goal firing in the mPFC (Hok et al., 2005) also includes a temporal component during the 2 s delay, mPFC activity was recorded as rats solved a variant of the task (Burton et al., 2009). Rats were trained every day to locate the goal zone in two conditions, a cue condition (the goal was directly signaled by a salient cue put on the ground of the arena) and a no-cue condition (i.e., in the standard place navigation task). In addition, the goal zone changed every day, thus emphasizing the time component of the task. Prefrontal neurons exhibited much less spatial selectivity in this variant than in the original place task (Hok et al., 2005), an effect likely due to the daily shift of the goal location. In contrast, many cells were observed to fire in a strong temporal relationship with the waiting period (see Fig. 2(c)). This firing pattern closely resembled the firing pattern observed in hippocampal place cells, with a peak of activity just before the end of the 2 s waiting period. Interestingly, lesion of the ventral hippocampus, the source of hippocampal connections to the mPFC, both abolished mPFC time-related activity and altered behavioral performance of the task (Burton et al., 2009). Although the rats were still able to localize the goal zone, they displayed a tendency to leave it prematurely, before the end of the 2 s, which prevented them from receiving the reward. This behavioral alteration suggests a deficit in the temporal prediction system and supports a role of the prefrontal cortex in controlling motor behaviors based on temporal predictions provided by hippocampus. In contrast, mPFC inactivation fails to alter either the performance of the continuous place navigation task or the goal-related firing of hippocampal place cells (Hok, Chah, Save, & Poucet, in press). This finding suggests that, once the task is well learned by the animal, normal function of mPFC is not required.

3. Neural network model

To account for the above-mentioned neural properties of mPFC neurons and hippocampal place cells in the continuous place navigation task, we propose a new neural network model endowed with the ability to perform spatial navigation (going to the goal) and temporal coding (waiting at the goal for 2 s). Although in our model these two abilities depend on the hippocampus, we also model the interactions between the hippocampus and mPFC in order to produce hippocampal secondary place fields and medial prefrontal goal firing.

The new model proposed here is based on two distinct previously published models that are summarized in Sections 3.1 (for spatial navigation and the cognitive map) and 3.2 (for temporal prediction). In the following we first shortly present these components, before explaining the new global model in Section 3.3.

3.1. Spatial navigation model

Terminology. In the following, we use the term *state* whenever a neuron or a set of neurons is activated, whatever the reason (place, timing, etc.). When dealing with spatial information, the state of a neuron may code for a *place* ("Place cell"). Concerning temporal information, a state is corresponding to either the current information about the environment (sensory state in EC), or the prediction of this information. In both cases, we build *transitions* between states which are coded on one neuron ("Transition cell", see below).

In all our models, neurons are modeled as analog units. However this single neuron activity is representative of what is assumed to be a population code in-vivo (see Section 5 for a discussion). According to Gaussier, Revel, Banquet, and Babeau (2002) (see also Fig. 3), sensory states are built in the entorhinal cortex using multi-modal input from the perirhinal and postrhinal cortices. This information is then transmitted to CA3 both by a direct pathway and through DG. In this case DG acts as a memory of previous states of EC allowing CA3 to associate the current state in EC with its previous state. In a more realistic model, DG granule cells should also perform some pattern separation and completion from sparse data in EC. For the sake of simplicity, this property is not present in this model (Banquet, Gaussier, Quoy, Revel, & Burnod, 2005). The architecture is consequently able to associate a neuron in CA3 with the transition between states (Banquet et al., 1997), thus creating a transition cell. After learning, it can reuse this information to predict in CA3 the available transitions from its current sensory state in EC. Once transmitted to CA1, one of these transitions is selected through a Winner-Take-All (WTA) mechanism. The need for the hippocampus to encode transitions between states rather than just states arises from the inability for a state-action coupling system to choose between two actions for the same state without using of an external supervising mechanism. The concept of transition cell will be further discussed in Section 5.

Therefore, in the architecture used in mobile robot navigation (Gaussier et al., 2002, see Fig. 3) EC sensory states are triggered by visual input and result in purely spatial coding by EC place cells. DG is a simple memory of the last place. The place field is easily identified by a WTA competition among place cells firing depending on the position of the agent. DG thus serves the sole purpose of memorizing the last winning place cell, allowing CA3 to associate it with the new winner of the competition. The system learns transitions from one place to another (e.g. place A to B) but contains no other temporal information than "place A came before place B". Place fields are present in the hippocampus and entorhinal cortex: large, stable place fields in EC (i.e. the place cells in our model) and





Fig. 2. Secondary field activity at the goal location for hippocampal CA1 place cells (from Hok et al., 2007). (a) Spatial activity of several recorded place cells. The circle marks the goal location. (b) Cumulative PETHs for all recorded place cells at the goal. (c) Raster plot and PETH for a mPFC neuron (from Burton et al., 2009).

narrow, context-dependent place field in areas CA3 and CA1 (i.e. transition cells).

The size of the place field is also dependent on how many place cells are coding for the environment. Recognition of a learned place is performed by comparing the new sensory information (only vision in this case) with the stored one. If this difference is above a given threshold, called the vigilance threshold, then a new place cell in EC is recruited for coding this new environment.

In our recent work (Cuperlier, Quoy, & Gaussier, 2007; Gaussier et al., 2002), the transitions learned in the hippocampus are also used by the prefrontal cortex (or parietal cortex, see Section 5 for a discussion) to build a cognitive map (see Fig. 3). In this map, consecutive transitions are linked together creating a graph where the nodes are the transitions, and the links the fact that one transition was activated after another. An association is also learned between a drive (the need to satisfy a goal, for instance going to a food location) and transitions immediately leading to the satisfaction of the goal. As this drive grows, the activity is propagated through the map, allowing the agent to plan the optimal path in terms of transitions to reach the goal in a way similar to gradient ascent. In that model, goals are coded and processed at the level of the mPFC. Information about the available transitions is passed on from the hippocampus to the nucleus accumbens (ACC) which performs action selection. In addition to this information, afferent connections



Fig. 3. Sketch of the transition learning and cognitive map architecture used in navigation in the model by Cuperlier et al. (2007). The current place is coded in EC. A WTA competition ensures that only one neuron in EC is active. The previous place is coded in DG. A neuron in CA3 codes for the co-activation of a current place in EC and a previous place in DG. This neuron is called a "transition cell". CA1 codes all possible transitions from the current place. All transitions are also coded on a cognitive map in mPFC. This map links the successive transitions ("AB" is linked with "BC" for instance). Activating a goal through a drive neuron (going to a food source for instance) activates the graph of transitions in the map. This activity biases the predicted transitions in ACC. This enables to perform the transition leading to the current goal. Abbreviations are as in Fig. 1. The arrowheads indicate the transmission of neuron states.



Fig. 4. Spectral timing model. Multi-modal signals (e.g. vision, sound, odometry, etc.) are integrated in EC. A WTA competition ensures that the activity of the most active neuron is transmitted to DG. Contrary to the previous model where transitions were learned in CA3 (see Section 3.1), here CA3 learns to *predict* the next EC state depending on the timing elapsed. Transitions between EC states are learned in CA1 where the memory of the current EC state comes from EC (perforant path) and the predicted EC state comes from CA3. A Winner-Take-All mechanism in ACC enables to select the most active transition and the corresponding motor action. The state of CA1 neurons and learning on the links coming from CA3 are given in Eqs. (5) and (6) respectively. The state of CA3 neurons and learning on the links coming from DG are given in Eqs. (7)–(10).

from the prefrontal cortex are used to bias the activity of the transitions and to select the optimal action to reach a goal through a WTA competition (Cuperlier et al., 2007; Gaussier et al., 2002).

3.2. Sequence and time learning model

Another hippocampal model was used in sequence learning (Banquet et al., 1997; Gaussier, Moga, Ouov, & Banquet, 1998), The memory in DG is more elaborated and acts as a timer. It is composed of sets of granule cells with various response times. Each of these cells responds with a Gaussian-like activity curve, with means regularly spaced along the temporal axis. This model is inspired by the spectral timing model (Grossberg & Merrill, 1992; Grossberg & Schmajuk, 1989). A set of these cells in DG codes for one sensory state in EC and the summation of pattern of activity of the cell population gives an estimate of the time elapsed since the sensory state in EC was entered. Each new sensory state in EC activates its corresponding set and inhibits the previously active set, so only one set can be active at any time (see Fig. 4). In order to avoid the dynamical simulation of granule and mossy cells interaction, the equation for the activities of the neurons in one particular set can be formally summarized as follows:

$$x_i^{\text{DG}}(t) = f_i \cdot \exp{-\frac{(t - t_i^a - m_i)^2}{v_i}}$$
(1)

where x_i^{DG} is the activity of neuron *i* of DG, f_i the amplitude of the Gaussian for neuron *i*, t_i^a the last activation time for the set to which neuron *i* belongs, m_i the mean of the Gaussian and v_i the variance of the Gaussian.

The Gaussian function parameters are given for each neuron in a set in the following way:

$$m_i = (\Delta_i - I + 1)^{\frac{i}{n_c - 1}} + I - 1$$
(2)

$$f_i = \frac{1}{i} \quad \text{for } 0 < i \le n_C \tag{3}$$

$$v_i = (m_i \cdot \Delta_i \cdot V)^2 \tag{4}$$

where Δ_i is the length of time covered by the activity of a set, *I* represents the activation time of the first granule cell responding to the activation of its set, n_c is the number of granule cells in each set and *V* a parameter controlling the variance of the Gaussians.

Eq. (2) ensures that more cells code for the beginning of the time interval than for the end (see Fig. 5). Granule cells are ordered according to index *i*. When *i* is small, the amplitude of the response f_i is high (Eq. (3)), and the corresponding Δ_i is small. As *i* increases, so does Δ_i . Hence the variance of the Gaussian v_i also increases (Eq. (4)). Therefore, cells respond with decreasing amplitude f_i and increasing variance for longer time intervals. These two properties allow broader, less precise predictions for longer timings and



Fig. 5. Top: Activity of DG neurons that provide a temporal trace of the time elapsed since the set of granule cells corresponding to a sensory state in EC was triggered. There are more Gaussian peaks at the beginning of the interval. Bottom: Activity of CA3 pyramidal neurons that predict 3 different timings for expected EC sensory states. Dashed lines represent the actual timing of the arrival of new EC state that was learned. For each prediction a neuron is activated and reaches its maximum potential just before the expected time of EC state onset. Shorter predictions are more accurate according to Weber's Law. Note that CA3 neurons are now predicting an EC sensory state, and not a transition as in the spatial model (see Section 3.1). Parameters are the following: $\Delta_i = 10$ s, I = 0.1 s, $n_c = 10$, V = 0.06.

sharp, accurate prediction for short timings (see Fig. 5). The time span covered by a set is in seconds or tens of seconds, which is coherent with biological properties of such timing systems in the brain.

By learning the association between the time trace of a previous event in DG and the newly entered EC sensory state, we obtain in CA3 cells that predict the next EC state and also convey temporal information about the timing of the next expected EC state (Andry, Gaussier, Moga, Banquet, & Nadel, 2001; Andry, Gaussier, & Nadel, 2005; Gaussier et al., 1998) (see also Eq. (8) below). Therefore, CA3 neurons do not code transitions as in the previous model (see Section 3.1). An interesting property is that the predictions can reproduce biological observations and follow Weber's law: the longer the expected time the less accurate the estimation of the timing (see Fig. 5). After learning, when a new sensory state is present in EC, the activity in DG is set to this sensory state. The time trace in DG starts activating CA3 previously learned predictions originating from this EC sensory state. For instance, if event A occurs (represented as sensory state A in EC) then previously learned events C and B will be activated. Moreover, if event C occurs faster than event B then peak activity in CA3 for C will arrive sooner than peak activity for B (see Fig. 5). It is noteworthy that this pattern is similar to the recordings of time estimation activity in the hippocampus by Hok et al. (2007) and McDonald et al. (2011). The activity is bellshaped and reaches its peak slightly before the learned timing. This peak gives a precession signal predicting the instant of the transition. This architecture is especially important in sequence learning where a sequence of movements can be learned and repeated with a precise timing to reproduce a trajectory (Andry, Blanchard, & Gaussier, 2011).

3.3. A new global model of spatial and temporal learning

The continuous place navigation task cannot be solved by any of the previous models alone. Therefore, we now present a new global model unifying spatial and temporal learning and involving the hippocampus and mPFC.

In the spatial learning model (see Section 3.1), transitions were learned in CA3, and the predicted transitions were located in CA1 whereas in the timing and sequence learning model (Section 3.2), the predicted EC state (and not transition) was learned in CA3. In order to merge the two models, we have chosen the latter option. Thus, in the global model, learning and prediction of transitions between EC states are separated in two steps (see Fig. 6). A first layer of pyramidal cells in CA3 learns to predict the next EC states. For instance, the neuron in CA3 corresponding to state G is activated by any state in EC that occurs before G. The topology between EC and CA3 allows the model to learn predictions for multiple states in parallel, which is why secondary associations can be learned at the goal for the CA3 pyramidal neurons (see below). Contrary to the spatial navigation model (see Section 3.1) EC state prediction neurons in CA3 do not convey any information about the previous EC state. For instance, there is no difference between transitions AG and BG leading to state G. Therefore, if a neuron in CA3 is predicting the state G and the current state is A, we need to know that the predicted transition is AG so that an action can be directly associated with it. This is the function assigned to CA1 pyramidal neurons that receive EC state prediction from CA3 and information about the last state entered from EC. The model then reconstructs transition activity and transmits it to the cognitive map in mPFC, so that mPFC can use this information to plan future actions. Each time the EC state changes, a transition between EC states is performed and learning is triggered in CA1 pyramidal neurons. A recruitment process takes place in CA1, where a new neuron is recruited to code for the new transition between EC states if the maximal activity of the group of neurons is below a given threshold. This allows the system to recognize if a transition between EC states has been previously learned or not. Synaptic weights are modified only for the most activated neuron. The equations for the computation of the neuronal activity and learning are the following:

$$x_{i}^{CA1}(t) = f\left(\sum_{j} W_{ij}^{CA3-CA1} \cdot x_{j}^{CA3} + W_{ij}^{EC-CA1} \cdot x_{j}^{EC} - \theta\right)$$

with $f(x) = \begin{cases} 0 & \text{if } x < 0 \\ x & \text{if } 0 \le x \le 1 \\ 1 & \text{if } x > 1 \end{cases}$ (5)

$$\frac{dW_{ij}^{\text{CA1}}}{dt} = f(\epsilon(t) \cdot (\alpha \cdot x_j^{\text{CA1}}(t) - \gamma \cdot W_{ij}^{\text{CA3-CA1}}(t)))$$
(6)

where x_i^* is the activity of neuron *i* of structure *, W_{ij}^{X-Y} is the weight from structure *X* to structure *Y*, θ is the activity threshold used to inhibit neurons of CA1 that are not co-activated by CA3 and EC inputs, $\epsilon(t)$ is a neuro-modulation factor equal to 1 when a transition occurs and 0 otherwise, α the learning rate and γ a decay factor. Parameter values are: $\theta = 1$, $\alpha = 0.2$, $\gamma = 0.01$.

Fig. 6 represents the hippocampal network for the learning of timed transitions. Using this system, we allowed neurons in CA3 to encode precise spatio-temporal information rather than purely spatial or temporal information. To accommodate the learning of various signals, a learning equation for CA3 neurons, based on a Normalized Least Mean Square (NLMS) algorithm (Nagumo, 1967), was developed:

$$x_i^{\text{CA3}}(t) = f\left(\sum_j W_{ij}^{\text{DG-CA3}} \cdot x_j^{\text{DG}}(t-1) - \theta\right)$$
(7)

$$\frac{dW_{ij}^{\text{DG-CA3}}}{dt} = \alpha \cdot \eta_i(t) \cdot \frac{(x_i^{\text{EC}}(t) - x_i^{\text{CA3}}(t))}{\sum x_k^{\text{DG}}(t)^2 + \sigma_1} \cdot x_j^{\text{DG}}(t)$$
(8)

$$\eta_i(t) = |x_i^{\text{EC}}(t) - m_i(t)| + \sigma_2$$
(9)

$$m_i(t) = \gamma \cdot m_i(t - dt) + (1 - \gamma) \cdot x_i^{\text{EC}}(t)$$
(10)

where α is the learning rate, η_i a learning modulation, x_i^{EC} is the unconditional signal for the LMS. σ_1 is a small value used to avoid the divergence of the synaptic weights for very low memory values. m_i is a sliding mean of x_i^{EC} , σ_2 is a low value setting a minimal learning rate and γ a parameter controlling the balance between



Fig. 6. Model of associative learning in the hippocampus explaining the secondary place fields. The arrowheads indicate the transmission of neuron states. EC state prediction neurons in CA3 learn to predict future EC sensory states based on the DG memory, which provides the time elapsed since the beginning of the current EC state. Secondary predictions are learned when a new EC state (sound) occurs simultaneously with reaching the goal, by means of a feedback signal from the mPFC (drive satisfaction) to the EC. Each CA3 pyramidal cell corresponds to one predicted EC state. However, goal-related reward leads to a wide activation of EC states. During this phase, a CA3 neuron learns to code specifically for this prediction (i.e. predicts the hearing of the sound corresponding to the release of the food pellet when at the goal location). Moreover the width of the activation profile allows other CA3 cells to learn secondary prediction. This prediction shows as a secondary field when their activity is spatially recorded. All hippocampal neurons thus code for two different features: the genuine place-related prediction (primary place field) and the prediction of the sound signal produced by the activation of the food dispenser at the end of the 2 s period spent by the animal at the goal location (goal-related firing).

past and current activities in the computation of the sliding mean. Parameter values are the following: $\alpha = 0.5$, $\sigma_1 = 0.01$, $\sigma_2 = 0.001$, $\gamma = 0.5$, $\theta = 0.05$.

These equations make the system more sensitive to quick changes in the input signals, allowing transient signals to be quickly learned but slowly forgotten. This property is related to the role of the hippocampus in novelty detection. It is known that the hippocampus is involved in the memory of contextual or place novelty, but not in the memory for objects (Mumby, Gaskin, Glenn, Schramek, & Lehmann, 2002). These findings have led researchers to develop models of hippocampal encoding and retrieval based on novelty detection (Meeter, Talamini, & Murre, 2004). Such models rely on the role of acetylcholine, which modulates learning in hippocampal neurons and prevents interference between previously learned memories and new memories (Hasselmo & Schnell, 1994). However the long time course of acetylcholine modulation (Hasselmo & Fehlau, 2001) has led some researchers to rely on the phase of the theta rhythm for encoding and retrieval for short periods of time (Hasselmo, Bodelón, & Wyble, 2002). Our learning equation thus represents the ability of the hippocampus-septum system to quickly encode new information by acting as a novelty detector.

This new global model (see Fig. 6) is able to account for the outof-field activity in the hippocampus. When EC neurons coding for the goal place ("place G") and the sound are activated, then the global state in EC is "*Place* G + *sound*". This EC state occurs simultaneously with the goal-related reward because the sound (produced by the activation of the automated food dispenser) signals the availability of the reward and happens solely at the goal location. When the goal is satisfied through a reward (finding food, or hearing the sound of the automated pellet dispenser), then the drive disappears. This change of the drive from "on" to "off" is transmitted through the projections from the mPFC to EC, indifferently targeting the neurons coding for EC states (see Fig. 6). The reason for this non-topological feedback projection is the diversity of the coding between the mPFC and EC. If we accept the hypothesis that the mPFC codes for a motivational context related to the current task, the association between this context and EC states needs to be learned. When the goal of the motivational context is reached, mPFC–EC connections could learn to associate the context with the active EC states. Later the context could then selectively activate relevant EC states. The widespread activation of EC states would thus be a side effect of this learning process. Modeling the coding of motivational contexts and their associations with EC states is still ongoing work.

Activation of the EC states also leads to learning in CA3 neurons of the association between EC state *place G* coming from DG and EC state "*place G* + *sound*" coming from EC. Therefore, transition cells have learned a primary association (the association with the state they are normally linked with in CA3) and a secondary one (the association with the goal-related reward). The process for the learning of the secondary associations is shown in Fig. 6. All neurons in CA3 now also have the ability to predict the occurrence of the goal-related reward when entering the goal place. This accounts for both the out-of-field activity at the goal place for all cells recorded in the hippocampus and the fact that this activity persists after inactivations of the mPFC (Hok et al., in press). The latter is indeed necessary to learn the associations of a place with the goal-related reward but, once this is done, goal-predicting activation occurs at the level of the hippocampus.

Even though secondary learning of transition cells in CA3 and CA1 can account for the secondary fields recorded in CA1, another plausible explanation for the spreading of the predictive activity at the goal location could be the effect of CA3 recurrent connections. This would not remove the need for some feedback signal from the mPFC to the hippocampus during the learning phase, required to explain why this activity only occurs at the goal location. However this signal could be transmitted to CA3 to mark an important transition leading to a rewarding state, and trigger synaptic learning in the recurrent connections so that the transition cell would project widely to other transitions cells. Upon arrival at the goal location, the transition cell would then predict the arrival of a rewarding sensory event and spread that activity to other transition cells, thus creating a secondary firing field for those neurons.



(d) CA1.

Fig. 7. Spatial activity of various neurons during the experiment. Scale is normalized between 0 and 1. The circle indicates the location where the goal was learned (as a visual place). All CA3 and CA1 prediction cells display a main firing field for some location in the environment and a secondary firing field at the goal (see Fig. 2 for comparison with in-vivo recordings from a rat).

4. Experiments

We have implemented the global model (Section 3.3) in the rate-coded neural simulator Promethe (Lagarde, Andry, Gaussier, & Giovannangeli, 2008). Experiments were first conducted in a simulated open environment with 20 perfectly identifiable visual landmarks (and next confirmed by real robot experiments (see Fig. 10)). During the initial phase of the experiment, a simulated mobile robot was allowed to explore the environment. During this exploration, place cells were autonomously learned based on a minimum activity threshold, using information about visual landmarks. Information about the azimuth and identity of the landmarks is merged in a model of the perirhinal and postrhinal cortices to create the pattern used to encode a place cell (Banquet et al., 2005; Cuperlier et al., 2007). Transitions between these places were also learned by the hippocampal system using the system presented in this paper (see Fig. 7). Finally the transitions were linked together by the cognitive map to create a representation of the possible paths in the environment. The robot was given enough exploration time to form a comprehensive representation of its environment, mapping available paths and learning the actions to perform to move from one place to the other. An unmarked goal location was located in the bottom-left corner of the environment. In addition, an automatic system produced the sound signaling goal-related reward when the robot stayed in the goal zone for two seconds. During the exploration phase, the robot moved too fast to stay long enough on the goal zone to produce the sound, and consequently the robot had no knowledge of the goal in the environment. During the second part of the experiment, the robot was made to stop at the goal location by a direct supervision by the experimenter. After two seconds a sound was simulated, signaling the goal-related reward of the robot. The robot consequently learned to associate the prediction "goal \rightarrow sound" with the action of not moving. With the goal-related reward, the feedback from the mPFC to EC allowed secondary associations for CA3 pyramidal cells, leading to the secondary fields at the goal location. The activity of neurons located in various parts of the architecture was recorded throughout the whole experiment (see Fig. 7).

Spatial correlates of neuronal activity in EC before and after the WTA competition are represented in Fig. 7. Before WTA competition, EC place cells display broad and noisy place fields. The activity resulting from the WTA competition corresponds to much



Fig. 8. Spatial correlates of activity of an entorhinal neuron coding for the sound modality. The neuron firing pattern resembles that of a place cell even though it is triggered only by the sound.

narrower place cells. The width of the place fields is highly dependent on the number of place cells coding a particular environment, which is regulated by a vigilance threshold (see Section 3.1). Fig. 8 shows the spatial correlates of an EC neuron coding for the sound. Since the sound is always produced at the goal location, the neuron firing pattern resembles that of a place cell even though it is triggered only by the sound.

After competition, CA3 pyramidal cells display larger fields than EC cells because the former are state prediction cells, which predict the arrival in a place from neighboring places. Spatial activity clearly shows a secondary activity at the goal location even for cells with a main firing field away from the goal. This is due to the prediction of the perception of the sound while waiting at the goal location, learned by secondary association. In contrast, CA1 cells show a lower activity secondary field. Using information from CA3 state predicting cells and EC place cells, CA1 cells can identify which transition is being predicted. They mostly code for one transition from a place to another, so their place field is a subset of a CA3 field. CA3 prediction activity alone can excite CA1 cells to a lesser extent, which is why they retain the secondary activity (see Fig. 9). However this secondary activity is not propagated to the cognitive map, because it is below-threshold. A virtual lesion of the mPFC cuts the feedback link to EC. Hence in this case there is no secondary activity.

Fig. 9 shows the temporal pattern of activity of CA3 cells while at the goal. The bell-shape activity is a result of the spectral timing model and a peak of activity predicting the expected perception of the sound marks the prediction. The shape of the activity is similar to the activity recorded in hippocampal neurons in the rat during the same experiment. The prediction is higher for one particular neuron that codes explicitly for the prediction of the sound. In a real biological system, a population of neurons would certainly code this prediction. Other pyramidal cells emit the same prediction activity but with a lower rate of firing, due to the fact that this is a secondary association. These cells primarily code for other transitions in the environment.

Finally, we performed extinction trials when the expected reward was not given after the waiting period. Weights are decreasing and secondary activity hits noise level (Hirel, Gaussier, & Quoy, 2011).

The experiment is also currently tested on a real robot (robulab 10 by Robosoft, 2012) in an indoor office environment. Preliminary results show that we obtain the same neuronal activities as in the simulated environment (Hirel, 2011). In that experiment, without direct supervision, the robot will not wait long enough in the goal location to learn the task. Therefore, the experimenter makes the robot stop by staying in front of it. The obstacle avoidance system will prevent the robot from moving further and thus provides a basic interaction mechanism to teach the task. The robotic setup being used is shown in Fig. 10.

5. Discussion

Model significance. Originally, the aim of the model was three-fold:

- 1. To design a coherent architecture that combines the processing specificities of the different hippocampal fields. Here the one-way connectivity of the hippocampo-entorhinal loop (Gaussier et al., 2007) is devoted not just to spatial processing, but also to sequential temporal processing.
- 2. To insert this hippocampo-entorhinal loop into a hippocampocortical system that stores in the long term this spatiotemporal information in the form of a cognitive map usable for navigation.
- 3. To render the functioning of the whole system coherent and integrated, in order to serve as a control system for robotic artifacts evolving in real indoor or outdoor environments.

The hippocampal-entorhinal loop has been shown to integrate both allothetic (visual) and idiothetic (path integration, proprioception) information in a way that is capable to account for the generation of both grid cells and place cells (Gaussier et al., 2007). The concept of transition cells (Banquet et al., 1997; Gaussier et al., 2002) was found to be necessary for appropriate integration of allothetic and idiothetic information. More importantly, it lends itself to a straightforward implementation of the cortical cognitive map in relation to the motor actions required when decisions are to be taken at choice points. In the time domain, transition learning in the tri-synaptic hippocampal loop also allows to predict future events and to learn sequences of events.

Convergence between the global model and experimental observation. The global model presented here is grounded on recent experimental data (Burton et al., 2009; Hok et al., 2007, 2007, 2005) for which it provides mechanistic interpretation. These data are important for the general conception of the model because they confirm previous assumptions that contributed to its elaboration:

- One such assumption concerns the dual function of hippocampal principal cells which is not only spatial but also temporal as it has been suggested by several authors, among others (Banquet et al., 2005; Fortin, Agster, & Eichenbaum, 2002; Gilbert, Kesner, & Lee, 2001; McDonald et al., 2011). It is confirmed by recent results from Hok et al. (2007).
- A related assumption concerns the respective roles of hippocampus and mPFC during temporal assessment, which apparently are not symmetrical. The origin of the evidenced timing information is in question. It could be prefrontal, hippocampal or elsewhere in the brain. In the modeled hippocampal system and in particular in DG, granule cells-mossy cells loop where supposed to be the locus of time dependent activities. This choice is reinforced by the experimental results which show that the inactivation of mPFC has no effect on the temporal profile of the secondary field activity (Hok et al., in press). Conversely, hippocampal inactivation suppressed the temporal profile of the mPFC activity (Burton et al., 2009).
- The long-term cortical storage of the cognitive map including several spatial goals was an essential feature of the original model (Banquet et al., 2005; Gaussier et al., 2002). The experimental results confirm this specific role of the mPFC in rats during goal-oriented navigation which is to link together spatial information and valence information related to a stimulus (positive or negative reward). With regard to the neural substrate of the cognitive map it is plausible that the whole map could be stored in the posterior parietal cortex and only the elements relevant for the task at hand, such as the current goal of the animal,



Fig. 9. Activity of individual cells near the goal location in different regions. (a) Activity of individual CA3 pyramidal cells near the goal location. There is a primary wave of activity that predicts the upcoming occurrence of the sound, and which depends on the time spent at the goal. The peak of activity precedes the expected timing of the sound. Secondary sound predictions, given by most cells because of the secondary associations, show the same pattern of activity with a lower firing rate. Other transitions are also predicted (corresponding to transitions from the goal place to neighboring places). (b) Activity of the reward satisfaction signal in mPFC. (c) Activity of EC neurons before competition with primary response (top line), secondary response (other lines) and noise activity of neurons not coding anything in the task (activity below 0.2). There is a sound prediction activity at the end of the 2 s period. (d) Activity of EC neurons after competition. There is only one winner because the robot is not moving. There is a sound prediction at the end of the 2 s period. (e) Activity of CA1 neurons giving the possible transitions and the sound prediction. Without the secondary sound predictions (they are below threshold), these activities are the same for mPFC neurons of the cognitive map.

could be activated in the mPFC (Whitlock, Sutherland, Witter, Moser, & Moser, 2008).

• Finally, these results emphasize the role of the hippocampalprefrontal connections, which provide for both a bottom-up transfer of spatio-temporal information from hippocampus to mPFC, and a top-down semi-direct transfer of motivational or reward-related information from mPFC to the hippocampus. This top-down transfer is expressed under the form of secondary fields in hippocampal place cell activity.

Significance of the results for hippocampal and mPFC functions.

 Transient function of mPFC and hippocampus during learning. During conditioning paradigms such as trace eye blink conditioning and complex conditioning, forebrain structures, in particular hippocampus and mPFC, are necessary only during a transient period before the full acquisition of the conditioning response (Berger & Thompson, 1978; Oswald, Maddox, Tisdale, & Powell, 2010). This fact could explain why inactivation of the mPFC after overtraining does not suppress the secondary field activity of hippocampal place cells.

Secondary fields and their temporal aspect. In addition to their main place fields, hippocampal place cells display a secondary peak of activity at the goal location. This new finding suggests that the spatial function of hippocampal place cells is only one aspect of their attributes. Of course, because this secondary activity takes place when the animal is in the goal zone, it may have a spatial meaning. However, that this activity concerns most of the place cells that map the experimental arena attenuates the specificity of the conveyed spatial information. The temporal aspect of this activity is important, as it may predict the end of the 2 s period by its ramping profile. As such it is reminiscent of similar activities recorded in CA3 cells during trace eye blink conditioning (Berger & Thompson, 1978; Solomon, 1980). Nevertheless, this secondary, goal-related place cell activity could also be interpreted as a learning signal indicating that the goal has been reached. Making this information available to the hippocampus is useful since in our model the global



Fig. 10. Robotic setup used for the learning and reproduction of the continuous place navigation task. Walls are wooden panels. The white square is the goal location. It is not used by the robot, but serves as a trigger for the sound after 2 s. It also enables the experimenter to see if the robot is staying at the goal location or not. Boxes are not landmark cues. They are obstacles that may be moved around.

cognitive map (where the goals could be represented) is assumed to be located only in the cortex.

Temporal profiles of mPFC neurons supposed to encode for transitions follow the temporal profile of CA1 neurons. Therefore an anticipatory activity is reported in the mPFC and in the hippocampus (Burton et al., 2009). The same authors also find in the mPFC an activity corresponding to the reward satisfaction signal arriving when the sound is perceived.

- *Main place fields in different hippocampal structures.* With regard to spatial information coding, our model posits the existence of large, stable place fields in the entorhinal cortex (i.e. the place cells in our model) and narrow, context-dependent place field in areas CA3 and CA1 (i.e. transition cells) (see Fig. 7 which shows EC place fields before and after competition, and Banquet et al., 2005). Although we cannot compare these results to those reported in Hok et al. (2007, 2007, 2005) who did not record EC cells, lesion studies indicate that the medial EC is involved in the detection of spatial novelty whereas the lateral EC is involved in the detection of both spatial and non spatial (object) novelty only when the environment is complex (Hunsaker, Mooy, Swift, & Kesner, 2007; Parron & Save, 2004; van Cauter et al., 2013). Furthermore, activation of lateral EC following new visual cues is also reported in c-fos studies (Jenkins, Amin, Pearce, Brown, & Aggleton, 2004; Van Elzakker, Fevurly, Breindel, & Spencer, 2008; Vann, Brown, Erichsen, & Aggleton, 2000) as well as neurophysiological recordings (Deshmukh, Johnson, & Knierim, 2012; Deshmukh & Knierim, 2011). These properties of the lateral and medial entorhinal cortices were modeled by Gorchetchnikov and Grossberg (2007) (see below paragraph on related models).
- Transition cells. The concept of transition cells emphasizes the spatio-temporal aspects of hippocampal processing and has received some experimental support. For instance, recent results suggest that the hippocampus does not only encode places but also accessible paths in the environment (Alvernhe, Cauter, Save, & Poucet, 2008). In this study, opening a shorter path in a well-explored maze strongly affects place cell activity in the vicinity of the novel shortcut. Transparent walls were used to dismiss the hypothesis that place cells were affected by visual changes in the environment caused by the new shortcuts. Oriented place fields may also be interpreted in terms of transition cells in constraint environments (Markus et al., 1995; Muller, Bostock, Taube, & Kubie, 1994) or when going to a goal (Samsonovich & McNaughton, 1997). Wiener, Berthoz, and Zugaro (2002) suggest that ordered activation of neurons having

adjacent or overlapping place fields may be achieved by synchronization with theta rhythm. The overlapping field between successively activated place cells could be the basis of transition cells. As stated by Markus et al. (1995) "it seems that place fields are more directional when the animal is planning or following a route between points of special significance". Transition cells are also akin to the reported retrospective and prospective cells that seem to code either previous or future trajectories to be taken. On a short time-scale, hippocampal place responses have been shown to be modulated by the immediately previous or imminent trajectory of the rat in a maze (Ainge, Tamosiunaite, Woergoetter, & Dudchenko, 2007; Ferbinteanu & Shapiro, 2003; Johnson & Redish, 2007; Wood et al., 2000). Prospective activity can also be demonstrated as the rat is forced to wait between trials (Ainge et al., 2007), but only if the task requires the rat to make a memory-based choice (Gupta, Keller, & Hasselmo, 2012; Pastalkova et al., 2008). This so-called delayed activity could provide a potential key to the mechanisms that bridge temporal gaps on a time scale of seconds and minutes. It is tempting to consider this as a temporary memory buffer of the behavior to be executed, or even a possible locus for the decision mechanisms. The report of prospective activity at choice points (van der Meer & Redish, 2010) may also be a signature of possible transitions from the current location. In our model, these possible transitions are located in CA1. The mPFC is biasing these transitions in the ventral striatum in order to allow for only one choice (Banquet, Gaussier, Quoy, Revel, & Burnod, 2004; Poucet et al., 2004). Transitions also enable a straightforward implementation of the Q-learning algorithm as developed in Hirel, Gaussier, Quoy, and Banquet (2010).

Finally, it is important to note that, in our view, transitions could be conceived as a sliding window of activation in a whole cell population rather than being encoded by individual cells (Harvey et al., 2012; McDonald et al., 2011).

The activity of our CA3 prediction cells, as well as CA1 transition cells (see Fig. 9), may be related to "time cells" as reported by McDonald et al. (2011). These cells correspond to particular key moments in a task and they can "retime" when a key temporal parameter is altered just as our cells if the delay period is modified. These time cells may also disambiguate overlapping sequences. However our model only codes transitions and not sequences. Closing the loop between the Subiculum and EC would be a step towards learning "transitions of transitions", thus the beginning of a sequence. Fig. 9 also shows that several cells respond in parallel near the goal location. Only one is winning because it has learned the timing of the expected event. All these cells could be viewed as "goal cells" (Okatan, 2010; Viard, Doeller, Hartley, Bird, & Burgess, 2011).

Predictions. The global model entails that timing is achieved in DG granule cells. Therefore, lesions of DG should be detrimental to timing activity unless other structures shown to be important for timing (such as the striatum or the cerebellum Drew et al., 2007; Thier, Dicke, Haas, & Barash, 2000) overcome this deficit through a circuit not based on the hippocampal tri-synaptic loop. In contrast, DG lesions should not impair the learning of transitions in CA1 because they rely on the current state in CA3 and the previous state in EC. Furthermore, without DG and CA3, the perforant path from EC to CA1 could create place cells in CA1 (copy of the EC state). Therefore, CA1 neurons should be more resilient to changes in new paths or a remapping of the environment as observed in Alvernhe et al. (2008). However, learning transitions in CA1 would need to have more than one winner in EC because the direct pathway from EC to CA1 carries information about previous EC states, and without CA3, there is no prediction of a next EC state. Therefore, navigation tasks should be impaired as reported in Brun et al. (2002).

Our model addresses the functioning of the hippocampoprefrontal loop in the steady-state when the task is well learned and perfectly performed by the agent. It is therefore likely that manipulations that would make the task less automatic, such as changing the location of the goal zone from one session to the next, should still require the integrity of the mPFC-hippocampal loop. More specifically, we predict that inactivation of the mPFC should prevent the development of the secondary fields in hippocampal cells, contrary to when the task is performed automatically during overtraining. Our model also predicts that the secondary temporal activity observed for hippocampal place cells should be stronger in CA3 pyramidal cells than in CA1 because of the spatial context coming directly from EC to CA1. Hippocampal prediction cells also have the property of having broader and less precise fields in CA3 than in CA1 (see Fig. 7).

Related models. Samsonovich and Ascoli (2005) have proposed a model of the relationship between the spatial and the memory functions of the hippocampus. In their model the connectionist part is limited to CA1 and CA3, where CA3 codes for the recently active place cells and CA1 for the future goal. The gradient of firingrate distribution of each place cell is used by an external "control module" for determining the direction towards the goal. They do not take into account the timing properties of the hippocampus.

In the model by Hasselmo and Eichenbaum (2005) EC layer III stores all possible sequences (which is the role devoted to CA3 coding transitions in our global model) and EC layer II stores the path previously taken. All information coming from EC is merged in CA1 cells, which learn to fire depending on the previous sequence.

Yoshida and Hayashi (2007) have designed a model where CA1 neurons learn to respond to a sequence of inputs in CA3, and not EC. Activation of a pool of CA3 neurons leads to the sequential activity of pools of neurons in CA1.

Lisman, Talamini, and Raffone (2005) propose a model of sequence learning and phase precession. Like in our model, it is based on interactions between DG and CA3. There is however no spatial response.

Finally, some models have implemented directional place cells in order to bridge the gap between the place cell and the direction to take in order to go to a particular goal location (Brunel & Trullier, 1998; Chavarriaga, Sauser, & Gerstner, 2003; Gerstner & Abbott, 1996; Hafner, 2000).

None of these models take into account both the spatial and temporal processing properties of the hippocampus. To the best of our knowledge, only Gorchetchnikov and Grossberg (2007) proposed a model of EC–DG learning of space and time. Spatial activity comes from medial entorhinal grid cells to DG. At the same time, the timing of event information from lateral entorhinal cue cells is coded in DG. They use grid cells whereas we only use place cells. However, in their model, convergence on CA3 is still to be done, as well as modeling CA1 and the mPFC.

Shortcomings. Our model has some limitations. First, there is no strong experimental support for time batteries to be localized in DG granule cells. We could however make some parallel with cerebellar granule cells providing the timing of movements (Thier et al., 2000).

Lesion simulations remain to be done. They are not straightforward for several reasons. First our model only relies on WTA mechanisms. For instance, we would need several winners in EC in order to be able to learn a transition in CA1 without inputs from CA3. The same holds true for predictions in CA3 when DG is lesioned. Thus, we would also need a population coding in the structures involved rather than one neuron corresponding to a state. Second, learning in CA1 is performed on the links between CA3 and CA1, and should also be done on the links from EC to CA1 in order to overcome a lesion of CA3. Similarly, learning should exist between EC and CA3 in order to overcome a lesion of DG. Third, it is possible that the EC-CA1-subiculum-EC loop could help in learning transitions when CA3 is lesioned.

Concerning the localization of the cognitive map, our model focuses on the mPFC while current literature emphasizes the role of the mPFC in working memory, and a role of the parietal cortex in goal navigation (Harvey et al., 2012). Indeed, patterns of activation of neural assemblies in the posterior parietal cortex are consistent with the successive activation of neurons of our cognitive map. Therefore, it would be possible to upgrade the model so that the parietal cortex stores the whole map and only part of the map needed for the ongoing task could be "uploaded" in the mPFC (Viard et al., 2011).

The decrease in firing rate activity observed in the medial entorhinal cortex by Gupta et al. (2012) during a cue-delayed task is not yet reported by our model because we only consider excitatory activity coming from mPFC that is coding for the goal location. However, this reduced activity may be due to the decrease of some inputs to EC like reported by van Cauter, Poucet, and Save (2008) in CA1 and simulated in Bray-Jayet, Quoy, Goodman, and Harris (2010).

Our model implements analogical neurons (mean frequency activity) and does not use spiking neurons. The major reason for this choice is its simplicity for running in real time a control architecture of a robot. Furthermore we do not see the need (for now) to have spiking neurons in order to find the same behaviors as found by neurobiologists. Lastly, our model does not address the question of phase precession and oscillations in the theta and gamma range.

Future work. The hippocampal temporal predictions could be used in a variety of ways in bio-inspired robotic systems. In recent works, they have been used to predict the occurrence of different types of events (visual, proprioceptive) and the evolution of various signals (Hirel, Gaussier, & Quoy, 2010). In addition, the temporal predictions are necessary for the animal during extinction trials, i.e. when the reward is omitted at the end of the delay. Without an accurate time estimation mechanism, the rat would wait forever for its reward with no knowledge of the timing when the reward should have been expected. A non-occurrence detection system was recently developed and used to solve the continuous place navigation task with normal and extinction trials with a mobile robot (Hirel et al., 2011). In this model, the basal ganglia play an important role in associating predictions with satisfaction signals. By combining this model with a previously developed model of reinforcement learning in the basal ganglia (Hirel, Gaussier, Quoy,

& Banquet, 2010), we hope to obtain a detailed predictive model of the interactions between the hippocampus, the prefrontal cortex and the basal ganglia.

A model of grid cell activity using the hippocampal loop was later created and integrated to the place cell architecture to provide a more accurate spatial description of the environment (Gaussier et al., 2007). In this model, place cells are created as a combination of grid cells of different spatial frequencies. It was used in a navigation model that does not include the timing prediction (Jauffret, Cuperlier, Gaussier, & Tarroux, 2012). Therefore, integration of grid cells in the global model is still to be done.

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